

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 45460-PT	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/CA 00/ 01153	International filing date (day/month/year) 03/10/2000	(Earliest) Priority Date (day/month/year) 04/10/1999
Applicant GAN, Zhibo		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 00/01153

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 G01N33/543 G01N33/542 C12Q1/68 C12Q1/34

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 96 25665 A (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA) 22 August 1996 (1996-08-22)	1-9, 11
Y	the whole document ---	10, 12-25
X	WO 98 39471 A (TROPIX, INC.) 11 September 1998 (1998-09-11)	12-25
	the whole document ---	
Y	WO 99 32655 A (NEN LIFE SCIENCE PRODUCTS, INC.) 1 July 1999 (1999-07-01)	1-25
	the whole document ---	
Y	WO 96 08721 A (BIOCIRCUITS CORPORATION) 21 March 1996 (1996-03-21)	1-25
	the whole document ---	
	--- -/--	



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

20 February 2001

Date of mailing of the international search report

27/02/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Griffith, G

INTERNATIONAL SEARCH REPORT

International Application No

/CA 00/01153

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 98 16657 A (CHIRON CORPORATION) 23 April 1998 (1998-04-23) the whole document ---	12-25
Y	EP 0 309 230 A (M.L. TECHNOLOGY VENTURES, L.P) 29 March 1989 (1989-03-29) abstract ---	10
A	WO 90 12888 A (BIOCONTROL SYSTEMS, INCORPORATED) 1 November 1990 (1990-11-01) the whole document ---	1-25
A	EP 0 244 932 A (BOARD OF REGENTS THE UNIVERSITY OF TEXAS SYSTEM) 11 November 1987 (1987-11-11) the whole document ---	1-25
A	US 4 391 904 A (D. J. LITMAN ET AL.) 5 July 1983 (1983-07-05) the whole document -----	1-25

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

/CA 00/01153

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9625665	A	22-08-1996	AU 714839 B	13-01-2000
			AU 4982196 A	04-09-1996
			CA 2211972 A	22-08-1996
			EP 0809803 A	03-12-1997
			JP 11500223 T	06-01-1999
			US 6103217 A	15-08-2000
			US 6080423 A	27-06-2000
WO 9839471	A	11-09-1998	AU 6443498 A	22-09-1998
			EP 0972071 A	19-01-2000
WO 9932655	A	01-07-1999	US 5972595 A	26-10-1999
			AU 2000699 A	12-07-1999
			EP 1042500 A	11-10-2000
			US 6066446 A	23-05-2000
WO 9608721	A	21-03-1996	CA 2199149 A	21-03-1996
			EP 0781413 A	02-07-1997
			JP 10505904 T	09-06-1998
WO 9816657	A	23-04-1998	AU 4904397 A	11-05-1998
EP 309230	A	29-03-1989	AT 124143 T	15-07-1995
			AU 633474 B	04-02-1993
			AU 2554188 A	17-04-1989
			CA 1339872 A	19-05-1998
			DE 3854029 D	27-07-1995
			DE 3854029 T	26-10-1995
			DK 244889 A	20-06-1989
			EP 0638807 A	15-02-1995
			ES 2074051 T	01-09-1995
			FI 892435 A	19-05-1989
			JP 2503147 T	04-10-1990
			JP 2000350598 A	19-12-2000
			JP 2000350599 A	19-12-2000
			KR 9602561 B	22-02-1996
			NO 892043 A	17-07-1989
			PT 88562 A, B	31-07-1989
			WO 8902476 A	23-03-1989
			US 5639604 A	17-06-1997
			US 5948899 A	07-09-1999
			US 6004745 A	21-12-1999
			US 5283174 A	01-02-1994
WO 9012888	A	01-11-1990	AU 639237 B	22-07-1993
			AU 5655290 A	16-11-1990
			CA 2062753 A	28-10-1990
			DE 69020555 D	03-08-1995
			DE 69020555 T	02-11-1995
			EP 0470172 A	12-02-1992
			JP 3043063 B	22-05-2000
			JP 4504802 T	27-08-1992
			US 5403721 A	04-04-1995
EP 244932	A	11-11-1987	US 4859581 A	22-08-1989
			AU 609386 B	02-05-1991
			AU 6987087 A	17-09-1987
			DK 122087 A	04-12-1987

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

CA 00/01153

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 244932	A		FI 871039 A	11-09-1987
			FI 924243 A	22-09-1992
			FI 924244 A	22-09-1992
			NO 870977 A	11-09-1987
			NO 930635 A	11-09-1987
			US 5332812 A	26-07-1994
			JP 62265998 A	18-11-1987
			US 5262403 A	16-11-1993
<hr/>				
US 4391904	A	05-07-1983	US 4299916 A	10-11-1981
			US 5342759 A	30-08-1994
			US 4533629 A	06-08-1985
			US 4540659 A	10-09-1985
			US 5432057 A	11-07-1995
			AU 538687 B	23-08-1984
			AU 6132080 A	02-07-1981
			BR 8007330 A	30-06-1981
			CA 1138332 A	28-12-1982
			DE 3071340 D	20-02-1986
			EP 0032286 A	22-07-1981
			ES 495936 D	16-01-1982
			ES 8202364 A	16-04-1982
			IL 60817 A	29-02-1984
			JP 1030109 B	16-06-1989
			JP 1548194 C	09-03-1990
			JP 61269068 A	28-11-1986
			JP 1465415 C	10-11-1988
			JP 56092218 A	25-07-1981
			JP 63012260 B	18-03-1988
			MX 6798 E	25-07-1986
			US 5156953 A	20-10-1992
			US 4843000 A	27-06-1989
<hr/>				

PATENT COOPERATION TREATY

RECEIVED KEGB FEB - 6 2002 PCT ENTERED _____ CHECKED _____
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From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To: GALE, Edwin J. et al. KIRBY EADES GALE BAKER Box 3432, Station D Ottawa, Ontario K1P 6N9 CANADA
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NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing (day/month/year) 23.01.2002	
Applicant's or agent's file reference 45460-PT	IMPORTANT NOTIFICATION
International application No. PCT/CA00/01153	International filing date (day/month/year) 03/10/2000
Priority date (day/month/year) 04/10/1999	
Applicant GAN, Zhibo	

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/ <div style="display: flex; align-items: center;"> <div> European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 pmu d Fax: +49 89 2399 - 4465 </div> </div>	Authorized officer Danti, B Tel. +49 89 2399-8161
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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 45460-PT	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/CA00/01153	International filing date (day/month/year) 03/10/2000	Priority date (day/month/year) 04/10/1999
International Patent Classification (IPC) or national classification and IPC G01N33/543		
Applicant GAN, Zhibo		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 02/05/2001	Date of completion of this report 23.01.2002
Name and mailing address of the international preliminary examining authority: <div style="display: flex; align-items: center;"> <div> European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465 </div> </div>	Authorized officer Linker, W Telephone No. +49 89 2399 8703



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/CA00/01153

I. Basis of the report

1. With regard to the elements of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1,2,4-9 as originally filed

3,3a as received on 20/12/2001 with letter of 14/12/2001

Claims, No.:

1-25 as originally filed

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/CA00/01153

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-11, 19-21, 23
	No:	Claims	12-18, 22, 24, 25
Inventive step (IS)	Yes:	Claims	1-11
	No:	Claims	12-25
Industrial applicability (IA)	Yes:	Claims	1-25
	No:	Claims	

2. Citations and explanations
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

s separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. **PCT/CA00/01153**

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: WO 99 32655 A (NEN LIFE SCIENCE PRODUCTS, INC.) 1 July 1999
(1999-07-01)

D2: WO 98 16657 A (CHIRON CORPORATION) 23 April 1998 (1998-04-23)

The subject-matter of present claims 12-15 and 24 is already known from document D1, see in particular page 3, lines 6-15, 21 and 24, page 5, lines 5, 15-17 and 23, page 6, lines 1, 8, and 14-24, page 7, lines 1-7 and 12-14. Furthermore, the subject-matter of claims 12-18, 22, 24 and 25 is already known from document D2, see in particular page 2, lines 10-20, page 6, lines 14-16 and 18, page 7, line 6, page 8, line 10 and 14, page 9, lines 3-7. Thus, the present application does not satisfy the criterion set forth in Article 33(2) PCT because the subject-matter of claims 12-18, 22, 24 and 25 is not novel (or inventive according to Article 33(3) PCT).

While the applicant's observations have been considered, the previously expressed opinion is nevertheless maintained for the following reason:

The Applicant has pointed to differences between the prior art and the present invention, however, the wording of the aforementioned claims is such that the claimed subject-matter cannot be distinguished from the above state of the art.

Using respective substrates for the enzymes selected according to dependent claims 19-21 and 23 is not considered to involve an inventive step as the skilled person could expect that the method of D2 can also be applied to enzyme/substrate combinations different from those explicitly mentioned in D2.

The subject-matter of claims 1-11 appears not to be disclosed or suggested by any of the cited prior art documents, thus, the subject-matter of claims 1-11 appears to satisfy the criteria set forth in Article 33(2) and (3) PCT.

R Item VIII

Certain observations on the international application

The features mentioned on page 3, lines 22-24 (i.e. due to the uneven distribution of the label between surface and liquid in a vessel after completion of the reaction) and page 4, lines 3-4 (i.e. without an additional step) appear to be essential to the claimed method in view of the object indicated on page 3, lines 4-5. Thus, claims 1, 12 and 25 do not satisfy the criterion set forth in Article 6 PCT.

catalytic activity of an enzyme and not just the amount of the enzyme as a given amount of the enzyme may have a widely varying activity depending on reaction conditions.

International PCT Application No. WO 99/32655 filed in the name of Nen
5 Life Science Products, Inc. of Boston, Massachusetts, USA, published on
July 1st, 1999, relates to a method for analyzing a sample for the presence and/or
activity of an enzyme. The invention makes use of a hydrophobic layer formed on
a solid support, the hydrophobic layer incorporating by hydrophobic interactions
and amphipathic enzyme substrate labeled with a reporter on its hydrophilic
10 region. The hydrophobic material having the substrate disposed therein is
contacted with a sample and with a polar solvent, whereby enzyme present in the
sample cleaves the substrate and produces a labeled hydrophilic fragment, which
fragment migrates to the polar solvent. The presence of the reporter is then
detected in the polar solvent or in the hydrophobic layer.

15 International PCT Application No. WO 98/16657 filed in the name of
Chiron Corporation of Emeryville, California, USA, which was published on
April 23rd, 1998, relates to a method of screening a compound capable of
regulating protease activity by incubating a protease and a polypeptide in the
presence and absence of a test compound. The polypeptide comprises an anchor
20 region, a protease recognition site and a detectable signal region. The anchor
region is bound to a solid support and the protease recognition site comprises (a) a
protease cleavable peptide bond, and (b) at least three naturally adjacent amino
acids on each side of the cleavable peptide bond. The signal region bound to the
solid support is detected. Detecting an amount of the signal region bound to the
25 solid support in the presence of the test compound, which is greater or smaller
than an amount detected in the absence of the test compound, indicates that the
test compound is capable of regulating protease activity.

It is important for developing a method to reduce the step of the
measurement procedure.

3 a

DISCLOSURE OF THE INVENTION

This present invention is for a method referred to as non-separation heterogeneous assay that greatly simplifies the detection, identification, measurement of concentration and activity of biological substances. It is based on the change of the label signal due to the distribution of the label between a solid surface and liquid in a vessel after completion of the reaction among reactants. The method involves the coating of a reactant (labeled or unlabeled) onto a surface, addition of a sample with or without a competitor labeled using a label tag or unlabelled. The change of the label signal can be directly measured.

DETAILED DESCRIPTION OF THE INVENTION

- The present invention relates to a new method for the detection, identification, measurement of concentration and activity of biological substances, which is based on the change of the label signal due to the uneven distribution of the label between surface and liquid in a vessel after completion of the reaction among reactants.
1. An assay in which the surface of a vessel is coated with reactant 1 which is a binding ligand for reactant 3 being the labeled form of reactant 2. Competitive binding reactions between reactant 2 and reactant 3 for reactant 1 or between reactant

PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference 45460-PT	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/CA00/01153	International filing date (day/month/year) 03/10/2000	Priority date (day/month/year) 04/10/1999
International Patent Classification (IPC) or national classification and IPC G01N33/543		
Applicant GAN, Zhibo		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 02/05/2001	Date of completion of this report 23.01.2002
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Linker, W Telephone No. +49 89 2399 8703 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/CA00/01153

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1,2,4-9 as originally filed

3,3a as received on 20/12/2001 with letter of 14/12/2001

Claims, No.:

1-25 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/CA00/01153

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-11, 19-21, 23
	No:	Claims	12-18, 22, 24, 25
Inventive step (IS)	Yes:	Claims	1-11
	No:	Claims	12-25
Industrial applicability (IA)	Yes:	Claims	1-25
	No:	Claims	

- 2. Citations and explanations**
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

R Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: WO 99 32655 A (NEN LIFE SCIENCE PRODUCTS, INC.) 1 July 1999
(1999-07-01)

D2: WO 98 16657 A (CHIRON CORPORATION) 23 April 1998 (1998-04-23)

The subject-matter of present claims 12-15 and 24 is already known from document D1, see in particular page 3, lines 6-15, 21 and 24, page 5, lines 5, 15-17 and 23, page 6, lines 1, 8, and 14-24, page 7, lines 1-7 and 12-14. Furthermore, the subject-matter of claims 12-18, 22, 24 and 25 is already known from document D2, see in particular page 2, lines 10-20, page 6, lines 14-16 and 18, page 7, line 6, page 8, line 10 and 14, page 9, lines 3-7. Thus, the present application does not satisfy the criterion set forth in Article 33(2) PCT because the subject-matter of claims 12-18, 22, 24 and 25 is not novel (or inventive according to Article 33(3) PCT).

While the applicant's observations have been considered, the previously expressed opinion is nevertheless maintained for the following reason:

The Applicant has pointed to differences between the prior art and the present invention, however, the wording of the aforementioned claims is such that the claimed subject-matter cannot be distinguished from the above state of the art.

Using respective substrates for the enzymes selected according to dependent claims 19-21 and 23 is not considered to involve an inventive step as the skilled person could expect that the method of D2 can also be applied to enzyme/substrate combinations different from those explicitly mentioned in D2.

The subject-matter of claims 1-11 appears not to be disclosed or suggested by any of the cited prior art documents, thus, the subject-matter of claims 1-11 appears to satisfy the criteria set forth in Article 33(2) and (3) PCT.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/CA00/01153

Re It m VIII

Certain observations on the international application

The features mentioned on page 3, lines 22-24 (i.e. due to the uneven distribution of the label between surface and liquid in a vessel after completion of the reaction) and page 4, lines 3-4 (i.e. without an additional step) appear to be essential to the claimed method in view of the object indicated on page 3, lines 4-5. Thus, claims 1, 12 and 25 do not satisfy the criterion set forth in Article 6 PCT.

catalytic activity of an enzyme and not just the amount of the enzyme as a given amount of the enzyme may have a widely varying activity depending on reaction conditions.

It is important for developing a method to reduce the step of the measurement procedure.

DISCLOSURE OF THE INVENTION

This present invention is for a method referred to as non-separation heterogenous assay that greatly simplifies the detection, identification, measurement of concentration and activity of biological substances. It is based on the change of the label signal due to the distribution of the label between a solid surface and liquid in a vessel after completion of the reaction among reactants. The method involves the coating of a reactant (labeled or unlabeled) onto a surface, addition of a sample with or without a competitor labeled using a label tag or unlabeled. The change of the label signal can be directly measured.

DETAILED DESCRIPTION OF THE INVENTION

The present invention relates to a new method for the detection, identification, measurement of concentration and activity of biological substances, which is based on the change of the label signal due to the uneven distribution of the label between surface and liquid in a vessel after completion of the reaction among reactants.

1. An assay in which the surface of a vessel is coated with reactant 1 which is a binding ligand for reactant 3 being the labeled form of reactant 2. Competitive binding reactions between reactant 2 and reactant 3 for reactant 1 or between reactant